UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF GEORGIA

KATELYN WEILBRENNER, A MINOR AND DI ANN COURTOY, INDIVIDUALLY AND AS NATURAL MOTHER AND NEXT FRIEND OF KATELYN WEILBRENNER,	*	
	*	**CASE NO.**
Plaintiffs,	*	
	*	**7:08-CV-00023-HL**
v.	*	
TEVA PHARMACEUTICALS USA, INC.,	*	
Defendant.	*	

PLAINTIFFS' BRIEF IN RESPONSE TO TEVA PHARMACEUTICALS USA, INC.'S MOTION FOR SUMMARY JUDGMENT

I. INTRODUCTION

Drug makers are responsible for their products. This is especially true for injuries caused by dangerous side-effects they know or should know are associated with the use of their products. In this case, the defendant admittedly knew of the association between its drug, minocycline, and the potential for the development of pseudotumor cerebri (increased intracrnanial hypertension) in adolescent/teenage patients. [1]

Notwithstanding this knowledge, Teva admittedly never sent a single letter (e.g., "Dear Doctor" letter) or any information of any kind to any physician in the United States warning them of this danger.[2] Nor did Teva ever detail minocycline to physicians or

[1] Defendant's Response to Request for Admissions No. 9, Exhibit 1
[2] Defendant's Response to Plaintiffs' Request for Admissions No. 6, Exh. 2

otherwise send representatives to the offices of physicians to provide them with such information.[3]

The medical literature associating minocycline with pseudotumor cerebri ("PTC") in adolescent patients dates back over two decades.[4] Drug makers are held to the standard of an expert charged with the duty of surveillance of the world literature regarding reported patient cases or studies of serious adverse events/side-effects associated with the use of their product.[5] In Teva's case, according to its Director of Pharmocovigilence, Dr. Dennis Miley, surveillance and analysis of the world literature is done on a weekly basis.[6]

Defendant's label was inadequate and defective. It failed to warn of the association between its product, **minocycline**, and PTC (Teva's label refers only to tetracylines). It failed to warn of the association between its product and PTC in **adolescents** (Teva's label refers only to adults). It failed to warn of the association between its product and **permanent visual loss** (Teva's label refers only to non-specific, permanent "sequalae"). And, it failed to provide adequate directions for its use, i.e., that patients should be regularly checked for papilledema while taking the drug (Teva's label makes no reference to any form of patient monitoring while taking their product).[7]

Inasmuch as the Defendant attempts throughout its brief to place the duty and authority to change its label on the FDA (vis-à-vis its regulatory scheme), it is important to note that it was not until **after** the injury to Ms. Weilbrenner (2006) that Congress **first**

[3] Defendant's Responses to Plaintiffs' Request for Admissions No. 11, Exh. 3
[4] Sampling of Medical Literature, Exh. 4
[5] Dr. Dennis Miley, Teva's Director of Pharmocovigilance Deposition, pg. 14, Exh. 5; Borel v. Fibreboard Paper Products Corp., F.2d 1098 (5th Cir., 1973); Owens-Illinois v. Zenobia, 601 A.2d 633,639 (Md.1992); Foster v. American Home Products Corp. 29 F.2d 165 (4th Cir. 1994)
[6] Dr. Dennis Miley, Depo. pg.14, Exh. 5
[7] Defendant did not place its label in the Physicians Desk Reference (PDR), nor undertake any effort to communicate appropriate warnings or instructions on its use to physicians by other means.

gave the FDA statutory authority to require a manufacturer to change its label (2007). 121 Stat. 823.

Ms. Weilbrenner's primary care physician, Dr. Robert Hawes, was completely unaware of the danger and potential for permanent visual loss associated with minocycline when he prescribed it for the treatment of Ms. Weilbrenner's acne. Had he known of this danger he " would most likely not have prescribed minocycline to Ms. Weilbrenner." [8]

GEORGIA STRICT LIABILITY STATUTE

Generally stated, the purpose of strict liability under Georgia product liability law is to "ensure that the costs of injuries resulting from defective products are borne by the manufacturers that put such products on the market."[9]

GEORGIA FAILURE TO WARN CLAIMS

Under Georgia law, the failure to warn is a product defect.[10] Failure to warn claims can take two forms, to wit:

(1) The manufacturer fails to adequately communicate the warning[11]; or,

(2) The manufacturer fails to provide an adequate warning of the product's potential risks.[12]

Defendant, Teva Pharmaceuticals USA, Inc., has failed in both respects, although only one is necessary to prevail on the Plaintiffs' product liability claim.

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[8] Affidavit of Robert Hawes, M.D., Par. 2, Exh. 6; Depo. of Dr. Hawes pgs. 65, Exh. 7
[9] Charles R. Adams, III, Georgia Law of Torts §25-8, note 4, at 499 (2007 ed.)
[10] Beam v. Omark Industries, Inc., 143 Ga. App. 142, 147, 237 S.E.2d607 (1977)
[11] Wilson Foods Corp. v. Turner, 218 Ga. App. 74,75 460 S.E.2d 532 (1995); Folsom v. Kawasaki Motors Corp. U.S.A., 509 F. Supp. 1364,1378 (M.D. Ga. 2007) Swicegood v. Pavia, Inc., 543 F. Supp. 2d, 1351,1355 (N.D. Ga. 2008)
[12] Swicegood @ 1355

II. STATEMENT OF FACTS

Plaintiff, Katelyn Weilbrenner, was fifteen (15) years of age when she was prescribed Defendant's antibiotic, minocycline, for treatment of acne by her primary care physician, Dr. Robert Hawes. Her prescription was initially filled at the CVS Pharmacy in her hometown of Moultrie, Georgia (Colquitt County) on January 16, 2006. This prescription was refilled at the same pharmacy on February 28, 2006. [13]

On May 11, 2006, while taking Defendant's product, Ms. Weilbrenner was diagnosed with intracranial hypertension (hereinafter referred to as pseudotumor cerebri or "PTC"). Although, the medication was stopped on the day of her diagnosis, defendant's product had already caused Ms. Weilbrenner significant permanent, visual loss. She is now legally blind.[14]

Defendant has admitted it was aware of the reported association between the use of minocycline and the potential development of pseudotumor cerebri in adolescent patients well before the incident leading to Ms. Weilbrenner's permanent loss of vision.[15] Nevertheless, Defendant also admits it has never mailed any information to any physicians in the United States informing them of this association, nor advised them of the need to routinely check patients for papilledema (i.e., swelling of the optic nerve, a hallmark of PTC) while taking minocycline.[16] Moreover, Teva has not undertaken to provide such information to physicians since this incident causing legal blindness to Ms. Weilbrenner.[17]

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[13] CVS Pharmacy Printout, Exh. 8
[14] Dr. Chaum, Depo. pg. 142 Exh. 9; Dr. Newman, Depo. pg. 149, Exh. 10
[15] Teva's Response to Plaintiff's Request for Admissions No. 9, Exh. 1
[16] Teva's Response to Plaintiff's Request for Admissions No. 6, Exh. 2
[17] Teva's Response to Plaintiffs' Request for Admissions No. 12, Exh. 11

As to causation, and contrary to the assertions of the defendant, Dr. Hawes has testified he "would most likely not have prescribed minocycline to Ms. Weilbrenner" had he been made aware of the possibility of permanent visual loss from its use. And, "even in the unlikely circumstance that [he] might have prescribed Ms. Weilbrenner minocycline [he] would have instructed Ms. Weilbrenner and her mother to discontinue minocycline and return to [his] office immediately if she began to experience headaches or visual disturbances. [He] would also have insisted that Katelyn be regularly checked for papilledema while taking minocycline."[18]

This does not conflict with Dr. Hawes' deposition testimony,[19] nor with the standard for causation in Georgia. While the e-mails about which he was cross-examined demonstrated his reluctance to say with "absolute certainty" what he would have done, such is not at odds with what he "most likely" would have done. Accordingly, his affidavit both accurately reflects what he "most likely" would have done (had he been properly warned) and is entirely sufficient to meet the Georgia standard on causation.

Additionally, the facts contained in his affidavit which relate to the manner in which he routinely receives updated information from manufacturers about potential side-effects or adverse events associated a drug (i.e., "Dear Doctor" letters, medical alerts, etc.) and how he uses this information, (i.e., he relies upon the information provided in making initial prescribing decisions for patients and advising them on their medications), all go to matters he was not specifically asked about in his deposition. [20]

Consequently, under the facts of this case, had the defendant complied with its duty to warn, Ms. Weilbrenner would "most likely" never have been exposed to

[18] Affidavit of Robert Hawes, M.D. par. 3,4, Exh. 12
[19] Deposition of Robert Hawes, M.D., 48, lines 24-25, pg. 49, lines 1-12
[20] Affidavit of Robert Hawes, M.D. par. 5, Exh. 13

minocycline. However, even under the unlikely circumstance she had been prescribed it, she would have been monitored for papilledema and discontinued the medication no later than April 24, 2006 (when she first began experiencing severe, global headaches), well over two weeks before being diagnosed with PTC and consequent permanent visual loss.

Several physicians have opined that Ms. Weilbrenner's PTC and permanent visual loss were caused by minocycline, including a treating ophthalmologist, Dr. Donald Mirate,[21] a reviewing ophthalmologist, Dr. Edward Chaum [22], and a reviewing neuro-ophthalmologist, Dr. Nancy Newman (Director of the Neuro-Ophthalmology Department at Emory University Hospital).[23] Among other things, Dr. Newman is the co-editor of one of the leading textbooks on neuro-ophthalmogy in the United States entitled "***Walsh & Hoyt's Clinical Neuro-Ophthalmogy"*** (now in its Sixth Edition), the author of numerous articles published in well recognized "peer reviewed" medical journals (including the subject of PTC),[24] and a treating physician to many PTC patients over the course of her practice at Emory.

Dr. Chaum (Director of the Hamilton Eye Institute at the University of Tennessee) [25] and Dr. Newman have also opined that Ms. Weilbrenner is legally blind.[26],[27]

Dr. Newman is routinely called upon in her practice to determine whether or not a visually impaired patient is legally qualified to drive in the state of Georgia. She has

[21] Dr. Donald Mirate Depo. Pg. 23, Exh. 14
[22] Dr. Edward Chaum Depo. pgs. 148-149; 152-156, Exh. 15
[23] Dr. Nancy Newman, Depo. Pgs.127-128, Exh.16
[24] Curriculum Vitae, Nancy J. Newman, M.D., Exh. 17
[25] Curriculum Vitae, Edward Chaum, M.D., Exh. 18
[26] Dr. Nancy Newman Depo. Pgs. 146, Exh. 10
[27] Dr. Chaum Depo. pg. 142, Exh. 9

testified that Ms. Weilbrenner is not legally qualified to drive in Georgia (i.e., she has less than 140 degrees of contiguous field of vision).[28]

III. ARGUMENT AND CITATION OF AUTHORITY

Drug manufacturers are required to adequately communicate warnings of dangerous side-effects or potential risks associated with their drugs to physicians. Georgia adheres to the "learned intermediary rule". Physicians become learned intermediaries only when they receive adequate warnings from the drug manufacturer. Thom v. Bristol-Myers Squibb Co., 353 F.3d 848, 853 (10th Cir. 2003). The intermediary's actual knowledge of a specific danger is a "condition precedent" to the application of the doctrine. Stuckey v. Northern Propane Gas Co., 874 F.2d 1563, 1569 (11th Cir. 1989). In Georgia, the drug manufacturer is ultimately responsible for any failure to provide a legally adequate warning to physicians. Catlett v. Wyeth, Inc., 379 F. Supp.2d 1374, 1381 (M.D. Ga. 2004).[29]

Just a few months ago, in Stacel v. Teva Pharmaceuticals USA, Inc., 2009 WL 703274 (N.D. Ill. March 16, 2009), Teva made the same arguments as they have raised in this case (e.g., plaintiff's state law claims are preempted by federal law, state law claims create an impermissible conflict with federal law, generic manufacturers can never deviate from the labeling provided by the name brand manufacturer, state law claims obstruct the purposes and objectives of Congress, etc.). These issues and arguments were

[28] Dr. Nancy Newman Depo. Pge.146-147, Exh. 19

[29] Interestingly, in Catlett, a case in which the drug manufacturer had complied with its duty to warn and instruct physicians on the use of its product, the Court noted "The record shows that Wyeth sent out hundreds of thousands of "Dear Doctor" letters that regularly updated the doctors on the research and explained the risks of taking the in drug in question…Further, the letter [dated July 24, 1997] addressed to the "Health Care Provider"] informed doctors that it was not recommended for doctors to prescribe the concomitant use of the drugs with each other or other weight loss drugs to create the "fen-phen" combination. Id. at 1381,1382.

all rejected. Teva was represented by the same attorneys as in this case, Goodwin Procter LLP, New York, NY.[30]

In Stacel, the labeling and product safety information at issue was for the same Teva product as here, minocycline. In rejecting Teva's arguments, the Court stated:

> Although it is clear the Hatch-Waxman Amendment was devised to allow generic manufacturers to get their drugs to market both cheaply and quickly, this purpose was to be achieved by permitting manufacturers to forego duplicative clinical trials. **It was *not* to be achieved by permitting manufacturers to engage in negligent activities.** (emphasis added). Id. at *6.

In its decision, the Court also reviewed in detail the federal regulations that allow generic manufacturers to unilaterally change their labels, that is, without prior approval from the FDA (sometimes referred to as CBEs – "Changes Being Effected").

> The core of Teva's argument – especially after the Supreme Court's decision in Levine – is whether the CBE provisions that permit manufacturers to add additional warnings to their labels without prior FDA approval is exclusively available to name brand manufacturers, or if generic manufacturers may also utilize this process.
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> The CBE regulations appear at 21 C.F.R. § 314.70(c)(6)(iii), which is located in Subpart B of Part 314. Subpart B is generally applicable to *new* applications, whereas, Subpart C is applicable to *generic* (or, "abbreviated") applications. However, section 314.97, which is located within Subpart C, states that "The applicant shall comply with the requirements of 314.70 and 314.71 regarding the submission of supplemental applications and other changes to an approved abbreviated application." § 314.97. **In other words, the regulations affecting generic drug applications state explicitly that the CBE provisions apply to generic drug manufacturers just as they do to name brand manufacturers. Id. at *5.** (emphasis added).

While acknowledging that a generic manufacturer must first use the same label as the name brand manufacturer in the process of obtaining FDA approval of its Abbreviated New Drug Application ("ANDA")[31], the Court makes clear that once

[30] More specifically, Glenn S. Kerner, Joanne M. Gray and Yuliya Gerstberg Scharf, Goodwin Procter LLP
[31] After the FDA signs off on the drug and its label, the manufacturer must generally use the exact labeling that the FDA approved (referring to the name brand mfg. label). However, in limited circumstances the

approval is received, the generic manufacturer bears the responsibility for the content of its label at all times, thereafter:

> Although Congress intended for ANDA applicants to submit identical labeling to the FDA when seeking ANDA approval – see 21 U.S.C. § 355 (j)(2)(A)(v) – the statute is silent as to the manufacturer's obligation after the ANDA is granted. **But, 21 C.F.R. § 314.97 is not silent – it states that generic manufacturers are obligated to comply with the same CBE provisions as brand-listed manufacturers are.** Id at *6. (emphasis added).

> While it is likely that a generic manufacturer may be spared any risk of negligence liability *during the application process*, there is no basis to conclude that this protection against negligence suits continues after the ANDA is approved. Id. at *7.

In another Teva case, Kelly v. Teva Pharmaceuticals USA, Inc., et.al., Teva once again moved for summary judgment (to avoid its liability for its "failure to warn" in connection with injuries caused by their product, metoclopramide, generic Reglan) upon primarily the same theories as they have raised in this case, i.e., it cannot deviate from the name brand manufacturer's label and state law claims are preempted by federal law.

In Kelly, the Court similarly reviewed the labeling process for generic manufacturers when first seeking FDA approval of their Abbreviate New Drug Application (ANDA), along with their duties and responsibilities to revise their labels after approval is received:

> In the ANDA, the generic manufacturer must include a label proposal for the generic product that is the same as the label which was approved for the name brand drug. C.F.R. § 355(j)(2)(A)(v). After the name brand and generic manufacturers receive approval from the FDA, they must continue to revise their labels "to include a warning as soon as there is reasonable evidence of an

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manufacturer may change the labeling after providing the FDA with notice of the change, but prior to actual FDA approval of the change. 21 C.F.R. § 314.70 This section, referred to as the "change being effected" ("CBE") provision, may be utilized only to "add, or strengthen a contraindication, warning, precaution, or adverse reaction" … Id. at *3 (parenthetical language in footnote added).

> association of a serious hazard with a drug; a causal relationship need not have been established." 21 C.F.R. § 201.80 (e), 314.97. [32]

Similarly, too, the Court found that Teva could avail itself of the provisions allowing it to change its label to "add or strengthen a contraindication, warning, precaution or adverse reaction" prior to receiving FDA approval under 21 C.F.R. §314.70 (c).[33]

However, the Court took its analysis a step further when it addressed Teva's duty to seek a label change under the provisions of C.F.R. §314.70 (b), which requires FDA approval before making the change - if one were to assume "hypothetically" Teva could not unilaterally make the change:

> Even if the Court were to assume that Teva could not unilaterally make changes to its label through the moderate changes procedure, Teva still had the option and obligation to apply for a labeling change through the major changes procedure, through which the FDA provides for a prompt determination regarding the sufficiency of the link between the drug and the reported problem. See, 21 C.F.R. § 314.70(b)…. In this case, however, Teva never proposed any changes before the FDA, therefore, the FDA never had the opportunity to accept or reject a labeling change. Because the labeling change was never before the FDA, there is no conflict between state and federal law and preemption does not apply.[34]

The same is true in this case. Teva never requested a labeling change from the FDA. [35]

Two months ago, the Supreme Court of the United States in Wyeth v. Levine, 129 S.Ct. 1187 (decided March 4, 2009) held that FDA regulations do not preempt state law product liability claims. In Wyeth , a case in which the Plaintiff alleged the drug manufacturer failed to warn of the potential for injury associated with "IV-push" administration of Phenegran (an anti-nausea drug), the Court stated:

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[32] Kelly v. Teva, et.al., Superior Court of Middlesex, Commonwealth of Massachusetts (April 12, 2007); pgs. 9,10, Exh. 20
[33] Id. at pgs. 3, 4
[34] Kelly v. Teva, et.al., Superior Court of Middlesex, Commonwealth of Massachusetts (April 12, 2007); pgs. 9,10, Exh. 20
[35] Zwicker depo. pgs. 44-48, Exh. 21

> In short, Wyeth has not persuaded us that failure-to-warn claims like Levine's obstruct the federal regulation of drug labeling. Congress has repeatedly declined to preempt state law… We conclude that it is not impossible for Wyeth to comply with its state and federal law obligations and that Levine's common-law claims do not stand as an obstacle to the accomplishment of Congress' purposes in the FDCA (Food, Drug and Cosmetics Act). Id. at 1204. (parenthetical added).

Contrary to defendant's assertions, the Supreme Court decision in Wyeth is applicable to the preemption arguments it has raised in this case.

More specifically, Teva's arguments that the Plaintiffs' state law claims for "failure to warn" are pre-empted by federal law because (1) its product labeling had been approved by the FDA; (2) drug labeling is the responsibility of the FDA, not Teva; (3) Plaintiffs' state law claims create an impermissible conflict with federal law; (4) state law claims obstruct the purposes and objectives of Congress (Food, Drug and Cosmetics Act – "FDCA"); and, (5) changing their label would have subjected them to an enforcement action by the FDA, have all been rejected by the Supreme Court.

Among other things, the Court noted that Congress had not authorized the FDA to pre-empt state law in "failure to warn" cases and reiterated the longstanding rule of law that manufacturers bear primary responsibility for providing adequate safety information about their drugs (including the content of their labels), not the FDA.

> Wyeth suggests that the FDA, rather than the manufacturer, bears primary responsibility for drug labeling. Yet through many amendments to the FDCA and to FDA regulations, it has remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times…See, e.g., 21 C.F.R. § 201.80 (e) (requiring a manufacturer to revise its label "to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug"); § 314.80 (b) (placing responsibility for post marketing surveillance on the manufacturer); 73 Fed. Reg. 49605 ("Manufacturers continue to have a responsibility under Federal Law….to maintain their labeling and update labeling with new safety information"). at 1197,1198.

To put the Defendant's responsibility into further perspective, it is important to note that it was only **after the injury to Ms. Weilbrenner** that Congress **first** gave the FDA statutory authority to require a manufacturer to change its label (after the drug's initial approval). 121 Stat. 823. This was duly noted in Levine :

> In 2007, after Levine's injury and lawsuit, Congress amended the FDCA. 121 Stat. 823. For the **first** time, it granted the FDA statutory authority to require a manufacturer to change its drug label based on safety information that becomes available after a drug's initial approval. § 901 (a), id., at 924-926. Id. *10,11 (emphasis added). In doing so, however….it adopted a rule of construction to make it clear that manufacturers remain responsible for updating their labels. See, 121 Stat. 925-926." Id. at 1196.

Accordingly, at the time of Ms. Weilbrenner's injury (May, 2006) the FDA could not require a label change to Teva's product, only Teva could.

And, even today, with the FDA now having authority to require a label change, the Supreme Court makes clear that it is still the manufacturers' duty to update their labels.

To fulfill its duty, as described in Levine (i.e., to adequately warn of dangers associated with their product and update their labeling with new safety information – Levine at 1196, 1198), Teva had two options. It could avail itself of the process allowing it to change its label by first seeking approval of the FDA before making the change, 21 C.F.R. §314.70 (b), or it could have availed itself of the option to make the change "unilaterally", before getting FDA approval, by giving the agency thirty (30) days advance notice of the change 21 C.F.R. §314.70 (c)

Teva admits that the provisions contained in 21 C.F.R.§ 314.70 entitled "Supplements and other Changes to an Approved Application" apply to it (via the incorporating language of 21 C.F.R. § 314.97 pertaining to ANDA holders/generic

manufacturers). Specifically, Teva's Rule 30(b)(6) witness on FDA regulatory matters, Ms. Jean Zwicker – Director of Regulatory Affairs for Teva Pharmaceuticals USA, Inc., testified that the provisions of 21 C.F.R. 314.70 apply to Teva; and, that Teva uses a "CBE 30" [referring to the 30 day notice provision of §314. 70 (c)] customarily in many situations.[36]

Nevertheless, Teva argues that had they filed a supplemental application for a label change, there is no assurance it would have been granted; and, that in fact, the FDA would likely have pursued an enforcement action against them, including misbranding charges, revoked their ANDA, and forced them to remove their product from the market.

These same arguments were made in Wyeth, to which the Supreme Court responded, as follows:

> The FDCA does not provide that a drug is misbranded simply because the manufacturer has altered an FDA-approved label; instead, the misbranding provisions focuses on the substance of the label and, among other things, proscribes labels that fail to include "adequate warnings." 21 C.F.R.§352(f) …..**the very idea that the FDA would bring an enforcement action against a manufacturer for strengthening a warning pursuant to the CBE regulations is difficult to accept --- neither Wyeth nor the United States has identified a case in which the FDA has done so**. Id. at 1197. [37] (emphasis added).

Interestingly, too, in Wyeth, the warning and drug safety information provided by the manufacturer included the specific side-effect and injury suffered by the plaintiff from exposure to their product (unlike Teva, who failed to warn of the specific injury, "permanent visual loss"). The only criticism in Wyeth was its failure to warn of the

[36] Jean Zwicker Depo. pgs.32-36, Exh. 22

[37] Notably, under the Food, Drug and Cosmetic Act (FDCA) 21 U.S.C.§301, et. seq., a drug is also misbranded when its labeling does not provide adequate directions for use. See, 21 U.S.C.§352. Teva failed to include in its label, or communicate to physicians by any other means, "adequate directions for use", i.e., recommending physicians regularly check their patients for papilledema while taking minocycline.

potential for injury resulting from a particular method of Phenergan administration ("IV-push"). Teva's labeling had far more defects.

Dr. Christopher Rhodes, who holds a doctorate degree in pharmacy, was a former member of the FDA Expert Advisory Committee on Generic Drugs. Over his forty (40) year career as a pharmaceutical scientist specializing in regulatory affairs, Dr. Rhodes developed a Doctoral Degree Program (PhD.) in regulatory affairs at the University of Rhode Island, while also frequently consulting with the FDA and others on "failure to warn" cases involving pharmaceutical products. He is presently Professor Emeritus at that institution.[38]

Generally, Dr. Rhodes has testified in this matter to the following, to wit:

(1) Teva's minocycline label was defective;[39] and

(2) Teva failed to adequately communicate to physicians the potential danger of PTC and permanent visual loss in adolescents from minocycline use, along with failing to provide them with sufficient and appropriate educational material)[40]

More specifically, Dr. Rhodes has indicated that Teva's label was defective and its communication of warnings to doctors was inadequate in the following respects, to wit:

(1) Minocycline was not specifically identified on its label, or otherwise communicated to doctors, as being a drug associated with the development of PTC;[41]

[38] Dr. Rhodes Curriculum Vitae, Exh. 23
[39] Dr. Rhodes Deposition, pg. 86, Exh. 24
[40] Dr. Rhodes Deposition, pgs. 86-87, Exh. 25
[41] It is important to note that Teva's label references "tetracyclines' as having been associated with the development of PTC only in "adults". Adults and adolescents (which are pediatric patients) respond differently to drugs. Similarly, all tetracyclines are not the same, as there are many drugs which fall within the family of tetracyclines and not all have the same properties, side-effects and risks associated with their

(2) The potential for the development of PTC in adolescents[42] (the primary patient population prescribed the drug for acne) was not included on the label, or otherwise communicated to doctors by Teva;

(3) The potential for permanent visual loss was not included on its label, or otherwise communicated to doctors by Teva;[43] and

(4) The need for patients to be routinely checked for the development of papilledema while taking minocycline was not included on its label, or otherwise communicated to doctors by Teva.[44]

At his deposition, Dr. Rhodes stated that "…Teva certainly had the right [and] the duty to contact FDA to try to get a change to the label. And I'm also relying on the fact that in certain circumstances Teva could have **unilaterally** changed the label to increase the strength of the warning." [45]

Dr. Rhodes testimony is consistent with the two options available to Teva to change its label, i.e., (1) the supplemental change process allowed under 21 C.F.R. §314.70 (b), whereby the drug manufacturer first seeks approval of a label change from FDA before making the change; or, (2) the "unilateral" means contained in 21 C.F.R. §314.70 (c), which allows the manufacturer to make a label change before FDA approval (i.e., upon giving thirty (30) days prior notice to the FDA of the change).

In substance, Defendant argues that as a generic manufacturer, the above two options are not available to it and proceeds to continue to advance the disingenuous

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use. Thus, the label failed to inform the physician that this particular family-member, minocycline, had been associated with the development of PTC and failed to inform the physician of its association within a patient population different from adults, namely adolescent/pediatric patients (like 15 year old Katelyn).

[42] Dr. Rhodes Deposition, pg. 113, Exh. 26
[43] Dr. Rhodes Depostion, pg. 113, Exh. 26
[44] Dr. Rhodes Deposition, pg. 114, Exh. 27
[45] Dr. Rhodes Deposition pg. 118, Exh. 28

argument that it may never deviate from the labeling of the brand name manufacturer. This is patently false. Every manufacturer is responsible for its own product, including its label (as well as communicating by other means appropriate drug warning and safety information – such as instructions on the safe use of its product – to physicians).

Manufacturers of generic drugs, like all other manufacturers, are responsible for the representations they make regarding their products.[46] When a generic manufacturer adopts a name brand manufacturer's warnings and representations without independent investigation, it does so at the risk that such warnings and representations may be flawed.[47]

Last year, in Swicegood v. Pliva, Inc., 543 F. Supp. 2d 1351, 1355 (N.D. Ga. 2008), a Georgia case against a generic drug manufacturer of metoclopramide (the generic version of name brand Reglan), the Court reiterated the longstanding rule that "Under Georgia law, a manufacturer may be held liable for failure to warn if it fails to (1) **adequately communicate the warning …** or (2) **fail[s] to provide an adequate warning of the product's potential risks**." (emphasis added), citing Watkins v. Ford, 190 F.3d 1213,1219 (11th Cir. 1999).

In Swicegood , also a "failure to warn" case, the Plaintiff sued the generic manufacturer, Pliva, Inc., but also the name brand manufacturers, Wyeth, Inc. and Schwarz Pharma., Inc. The Plaintiff's claim against the name brand manufacturers was based upon the erroneous theory (also advanced by Teva) that generic manufacturers cannot deviate from the content of the drug label provided by the name brand manufacturer. Since they could allegedly not provide any different warnings to

[46] Foster v. American Home Products Corp. 29 F.3d 165, 170 (4th Cir.1994)
[47] Id. at 169

physicians than those provided by the name brand manufacturer, the Plaintiff's argued the name brand manufacturers should be held liable for Pliva's defective label and failure to warn.[48]

This theory was unequivocally rejected by the Court, which indicated, inter alia, that generic manufacturers are solely responsible for their products and cannot shift responsibility for their failure to warn to any FDA regulatory scheme, name brand manufacturer, or anyone else:

> .…solely by providing the initial safety labeling, Wyeth and Schwartz did not assume the duty of labeling generic Reglan (citing, Smallwood v. U.S. 988 F. Supp. 1479,1482 (S.D. Ga. 1997)…After all, the generic manufacturer Pliva used its own label on its products, which it was free to alter with FDA approval. Id. at 1356.

Closer inspection demonstrates how strikingly similar and equally without merit Teva's arguments herein are to those raised in Swicegood. For example:

> The Plaintiff argues further that liability for brand name manufacturers is appropriate under the FDCA (Food, Drug and Cosmetics Act) because generic manufacturers are required to use the safety information provided by the name brand manufacturer **until the abbreviated new drug application is approved by the FDA.** (emphasis added)**.** It is true that Congress enacted the Hatch-Waxman Amendments to the FDCA with the goal of allowing generic manufacturers to [initially] rely on the safety information of the name brand manufacturer. (bracketed portion added).
>
> In this case, however, the Plaintiff concedes that the FDA long ago gave approval of the abbreviated applications for generic Reglan (***just as it did for generic Minocin, minocycline[49] - fourteen (14) years before Teva's product caused legal blindness to Ms. Weilbrenner***). As such, the generic manufacturer was not bound by Wyeth or Schwarz's label. Defendant had the ability – albeit with approval from the FDA – to 'add or strengthen a contraindication, **warning,** precaution, or adverse reaction' … (citing Colacico v. Apotex, Inc., 432 F. Supp. 2d 514, 523 (E.D. Pa. 2006) explaining the FDA's interpretation of 21 C.F.R. § 314.70 (c)(6)(iii)(A). Id. at 1358. (italicized portion and emphasis added).

[48] This is the same theory proposed by Teva in their effort to shift responsibility to someone else for their own "failure to warn" of dangers known by it to be associated with their product.
[49] Teva Pharmaceuticals USA, Inc.'s Memorandum of Law in Support of Its Motion for Summary Judgment, pg. 7, Section C

In effect, Teva's motion is seeking immunity for the injuries caused by their defective labeling and failure to warn - knowing full well that neither the name brand manufacturer, FDA, nor anyone else is liable for their conduct.

The Swicegood approach does not differ from many other courts nationwide. These cases typically follow the holding and rationale provided in the seminal case, Foster v. American Home Products Corp., 29 F.3d 165 (4th Cir. 1994). In Foster, the Court, likewise, rejected the idea of holding the name brand manufacturer liable for an injury caused by a generic company's failure to warn, as well as rejecting the notion that generic manufacturers are forever bound to the label and safety information provided by the name brand manufacturer (insulating them from state law failure to warn claims).

In Foster, the Court acknowledges that a generic manufacturer must show "equivalency" in a number of ways with a prior approved name brand product (including initially using the same label) in its application to obtain approval from FDA of its Abbreviated New Drug Application ("ANDA"). Accordingly, the Court observed:

> The generic manufacturer must use the same labeling as the previously approved equivalent drug. **However, manufacturers of generic drugs approved pursuant to ANDAs (*like Teva*) may alter a drug's labeling to add or strengthen a contraindications, warning, precaution or adverse reaction….** Id. at 169. (emphasis and parenthetical added). The statutory scheme governing premarketing approval for drugs simply does not evidence a Congressional intent to insulate generic drug manufacturers from liability for misrepresentations regarding their products, or to otherwise alter state products liability law. Id. at 169. (emphasis and italicized parenthetical added).

The Court also addressed the inherent risk taken by generic manufacturers who choose to follow the content of a name brand manufacturer's warning after approval of its ANDA, rather than exercise their own independent judgment to ensure that their warnings are adequate:

> When a generic manufacturer adopts a name brand manufacturer's warnings and representations without independent investigation, it does so at the risk that such warnings and representations may be flawed. In cases involving products alleged to be defective due to warnings "the manufacturer is held to the knowledge and skill of an expert…The manufacturer's status as expert means that at a minimum he must keep abreast of scientific knowledge, discoveries, and advances and is presumed to know what is imparted thereby." Id. at 169,170.

By contrast to the conduct of the Defendant in this case, the pharmaceutical company in Catlett v. Wyeth, Inc., 379 F.Supp. 2d 1374, 1381 (M.D. Ga. 2004) satisfied its duty to warn by informing doctors of the risks of the drug in question by sending out "thousands of 'Dear Doctor' letters." Moreover, the company's letters provided doctors with additional safety information about its use. Id. at 1381,1382. Teva did not.

Defendant alleges its label contained an adequate warning; and, therefore, they fulfilled their "duty to warn". This argument is misplaced. Teva's label was not adequate. But, more to the point, Teva breached its duty under Georgia law to adequately communicate effective warning and safety information to physicians.[50]

Defendant's sole causation argument is that Dr. Hawes did not read its label. Defendant never placed its labeling information in the Physicians Desk Reference ("PDR"); more importantly, Teva never provided adequate warning and prescribing information to Dr. Hawes (or any other physician in the United States) by any other means whatsoever.

Minocycline was originally sold under the brand name Minocin. It has been on the market for a number of years. Dr. Hawes was made aware of the product and its indicated uses during his training in medical school. He was familiar with the drug, had

[50] Swicegood at 1355.

prescribed it over the years and had previously read the label (though, understandably, he could not recall exactly when and where he read the label). [51]

Just like other doctors, Dr. Hawes must rely on drug manufacturers to advise him of information regarding potential serious side-effects associated with their products. Such information is routinely obtained and shared by manufacturers during the "post-marketing surveillance" period, i.e., the period of time after a drug has been approved by the FDA and reaches the market. Clinical trials performed prior to a new drug's approval only involve a relatively small number of "sample" patients by comparison to the number of patients who receive the drug after it is approved. Once a drug reaches the market, the number of patients exposed to the drug increases exponentially.[52] Consequently, it is only after the drug is on the market for many years that most serious adverse events (side-effects) are discovered.[53]

While drug manufacturers are allowed to add or strengthen a warning, precaution, or adverse reaction information to their label (which certainly serves the public interest in promoting drug safety), the labeling argument still misses the point. Communication of an adequate warning to physicians is what is most crucial (remembering that physicians do not fill prescriptions; and, consequently do not have the package inserts/drug labeling information at hand). It is essential that drug makers undertake reasonable steps to inform physicians of potential serious side-effects, including the initial signs or symptoms of a serious side-effect, and the appropriate testing, monitoring or examinations that should be done while the patient is on the medication (in order to prevent or at least reduce the likelihood of any serious damage and injury from the product).

[51] Dr. Robert Hawes Deposition, pg. 66, Exh. 29
[52] Jean Swicker Deposition, page 41, Exh. 30
[53] Dr. Rhodes depo., pgs. 92-93, Exh. 31

Physicians do not review the PDR for every prescription they make (particularly for drugs they have prescribed in the past, and about which they have not received any information concerning dangers not included on previous labels). Just the same, had Dr. Hawes looked to the PDR, he would not have found the Defendant's label. And, hypothetically speaking, even it had been there, Teva's label was woefully inadequate and defective. On the other hand, had Teva fulfilled its duty to warn, Dr. Hawes "most likely" would not have prescribed Ms. Weilbrenner minocycline.

It is undisputed that Teva never sought FDA approval of a label change for minocycline.[54]

Many other jurisdictions have held that even if the FDA regulatory scheme is construed to prevent a manufacturer from modifying an approved label without first obtaining FDA approval – the label is not the only means by which a warning can be communicated to a physician by a manufacturer. Specifically, the manufacturer can send "Dear Doctor" letters which are expressly permissible under the FDA regulations.

In Perry v. Novartis Pharma. Corp., 456 F. Supp. 2d 678 (E.D. Penn. 2006), the Court stated:

> Any restrictions that FDA may place on drug labeling do not prohibit manufacturers from disseminating evidence of a danger by other means. When it originally promulgated these regulations, the agency made clear that (*quoting the federal regulations*): These labeling requirements do not prohibit a manufacturer, packer, relabeler, or distributor from warning health care professionals whenever possibly harmful adverse effects associated with the use of the drug are discovered….the issuance of letters directed to health care professionals (e.g., "Dear Doctor" letters containing such information) is not prohibited by these regulations. 44 Fed. Reg. 37434, 37447 (June 26, 1979).
>
> Indeed, the FDA has promulgated particular regulations guiding the dissemination of information to health care professionals, see C.F.R.§ 200.5,[55] making it clear

[54] Zwicker Depo. pgs. 44, 48, Exh. 21
[55] 21 C.F.R. §200.5, Exh. 32

> that it expects such communication to take place. Id. at 682 (italicized portion added).

Moreover, state law may require a drug manufacturer to at least seek Food and Drug Administration (FDA) approval for the addition of a new warning where there has been no determination by the agency whether there is a link between the adverse health effect to be warned against and the use of the drug. Id. at 685.

To put it another way, the duty of the manufacturer is to "share what they know." Teva has admittedly never communicated any warning to any physician in the United States of the danger to adolescents associated with their product (i.e., developing PTC and permanent visual loss); nor, have they ever informed physicians of the need to monitor their patients for papilledema while taking their product.[56] Discontinuation of the product at the first sign of papilledema greatly reduces the likelihood that a patient's problem will be permanent, rather than temporary.

PUNITIVE DAMAGES CLAIM

OCGA § 51-12-5.1 provides for punitive damages in tort actions where the defendant's actions show willful misconduct, malice, fraud, wantonness, oppression or that entire want of care which would raise the presumption of conscious indifference to consequences. Such damages are awarded to penalize, punish or deter a defendant.

Inasmuch as this case arises out of a cause of action for product liability, there is no cap to be applied to the award. Plaintiffs are unaware, after having made reasonable inquiry, of any prior award in Georgia against this defendant for its drug product, minocycline.

[56] Teva's Response to Plaintiffs' Request for Admissions No. 9, Exh. 1 and Request for Admission No. 6, Exh. 2

Punitive damages are statutorily allowed upon proper proof by clear and convincing evidence that the defendant acted either willfully or with that entire want of care which would raise the presumption of conscious indifference to consequences. Plaintiffs' evidence in this case, insofar as Defendant's actions are concerned, is both clear and convincing – certainly to the degree that overcomes summary judgment.

Teva manufactured and sold its drug in Georgia. Plaintiff, Katelyn Weilbrenner, took defendant's drug and suffered permanent loss of vision to the extent that she is legally blind.

The uncontroverted evidence in this case is that defendant Teva's predecessor, Biocraft Laboratories, Inc., received FDA approval of its ANDA for 100 mg. Minocycline, the product taken by Ms. Weilbrenner, in 1992. A few years later in 1996, Biocraft (together with the Lemmon Company) formed the corporate entity Teva Pharmaceuticals USA, Inc.[57] (a wholly owned subsidiary of Teva Pharmaceutical Industries, Ltd. – one of the largest generic pharmaceutical companies in the world).[58]

For well over a decade after the formation of Teva Pharmaceuticals USA, Inc., the company failed to warn of the association between its product, minocycline, and PTC in adolescents. It failed to warn of the danger that patients could suffer permanent visual loss from taking their drug. It failed to provide adequate directions for its use, specifically, that physicians should regularly monitor their patients for papilledema while taking their product.

All this, despite the fact that the medical literature was replete with reported cases of patients suffering PTC associated with the use of minocycline (particularly, adolescent

[57] Teva Pharmaceuticals USA, Inc.'s Memorandum of Law in Support of Its MSJ – pg. 7
[58] Teva Pharmaceuticals USA Website - Corporate Profile, Exh. 33

females like Katelyn Weilbrenner)[59], receipt of adverse event reports, and its own admitted knowledge of the danger, "Teva admits that pseudotumor cerebri (PTC) is recognized as a potential adverse reaction to the use of minocycline…"[60] (parenthetical added).

Nevertheless, Teva made no attempt to revise its label nor communicate by any other means its knowledge of this danger or how to avoid injury to their patients by regularly checking them for papilledema while taking their drug[61] - which might well have prevented the precise injury suffered by Katelyn Weilbrenner - permanent visual loss and legal blindness.

Taken together, these facts, along with many others referenced hereinbefore, certainly present a jury question on the issue of punitive damages.

CONCLUSION

Applying the summary judgment standard to the facts and evidence presented in this case clearly demonstrates that Defendant's Motion for Summary Judgment be denied.

Respectfully submitted, this 25th day of May, 2009.

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[59] Journal Articles, Exh. 4
[60] Defendant's Response to Plaintiffs' First Request for Admissions No. 9, Exh. 1
[61] Defendant's Response to Plaintiff's First Request for Admissions Nos. 6, 11, Exh. 2 and 3

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